Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

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Hepatitis C

Overview of Disease State – Hepatitis C

- Hepatitis C virus (HCV) infection is the most common chronic blood-borne infection in the United States (US)
  - In approximately 15% to 25% of patients who become infected with hepatitis C, the virus is eliminated during the acute phase of the infection by T cell-mediated antiviral mechanisms; however, in the other 75% to 85% of patients, the HCV persists for decades
  - An estimated 23,000 to 46,000 children in the US have HCV
  - Approximately 2.7 million people in the US are chronically infected, although it is estimated that nearly 75% of these people may be unaware of their infection due to the insidious progression of the disease
  - HCV accounts for 40% of chronic liver disease in the US. In patients with chronic HCV infection followed for 20 years, disease progression to cirrhosis occurs in about 20% to 25%
  - Of those who develop cirrhosis, approximately 30% will develop end-stage liver disease over the next 10 years and 1% to 2% per year will develop hepatocellular carcinoma
  - HCV infection is the most common reason for liver transplantation and results in an estimated 8,000 to 10,000 deaths per year in the US
- The most important risk for HCV infection is injection-drug use, which accounts for at least 60% of acute HCV infections in the US
  - Other modes of transmission include mother-to-infant, receiving a blood or organ donation prior to 1992, occupational exposures, chronic hemodialysis, and contaminated devices shared for non-injection drug use, such as intranasal illicit drug use
  - Sexual transmission also occurs but generally seems to be inefficient except among human immunodeficiency virus (HIV)-infected men who have unprotected sex with men
  - Other risk factors include incarceration and receiving a tattoo in an unregulated setting
    - It is estimated that 29% of incarcerated persons in the North America are anti-HCV positive

Hepatitis C – Indications

Drugs	Generic	Indications
		Interferons
peginterferon alfa-2a (Pegasys)		Chronic hepatitis C (CHC) ▪Treatment of adults with CHC as part of a combination regimen with other hepatitis C virus antiviral drugs in patients ≥ 5 years old with compensated liver disease ▪Monotherapy is not recommended unless a patient has a contraindication to, or significant intolerance of, other HCV antiviral drugs Chronic hepatitis B ▪Treatment of HBeAg-positive and HBeAg-negative chronic hepatitis B in adults with compensated liver disease and evidence of viral replication and liver inflammation
peginterferon alfa-2b (PEGIntron)		Chronic hepatitis C ▪For patients with compensated liver disease in combination with ribavirin (Rebetol) and an approved Hepatitis C Virus (HCV) NS3/4A protease inhibitor in adult patients (≥ 18 years old) with HCV genotype 1 infection ▪For patients with compensated liver disease in combination with ribavirin (Rebetol) in patients with genotypes other than genotype 1, pediatric patients (3 to 17 years of age), or in patients with genotype 1 infection where the use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors Monotherapy should only be used in the treatment of CHC in patients with compensated liver disease if there are contraindications to, or significant intolerance of, ribavirin and is indicated for use only in previously untreated adult patients; Combination therapy provides substantially better response rates than monotherapy
		Ribavirin
ribavirin	**X**	Chronic hepatitis C ▪In combination with peginterferon alfa-2a (Pegasys) in patients ≥ 5 years of age with compensated liver disease and have not been previously treated with interferon alfa ▪Includes patients with histological evidence of cirrhosis (Child-Pugh A) ▪Includes adult patients with clinically stable human immunodeficiency virus (HIV) disease and CD4 count > 100 cells/mm^2 Ribavirin must not be used as monotherapy; Safety and efficacy have not been demonstrated with treatment longer than 48 weeks; Safety and efficacy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon therapy

Hepatitis C – Indications

Drugs	Generic	Indications
		Ribavirin (Continued)
ribavirin (Rebetol)	**X**	Chronic hepatitis C ▪In combination with interferon alfa-2b (pegylated [PEG-Intron] or non-pegylated [Intron-A®]) in patients (≥ 3 years of age) with compensated liver disease Rebetol must not be used as monotherapy Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection No safety and efficacy data are available for treatment of longer than 1 year
ribavirin (Ribasphere, Ribasphere RibaPak)	**X**	Chronic hepatitis C Capsules ▪In combination with interferon alfa 2b (pegylated and non-pegylated) in patients ≥ 3 years of age with compensated liver disease Ribasphere must not be used as monotherapy Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection; No safety and efficacy data are available for treatment of longer than 1 year Tablets ▪In combination with peginterferon alfa-2a (Pegasys) in adults with compensated liver disease and adults who have not been previously treated with interferon alfa ▪Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm2 Safety and efficacy data are not available for treatment longer than 48 weeks The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon Safety and efficacy have not been demonstrated for treatment longer than 48 weeks

Hepatitis C – Indications

Drugs	Generic	Indications
		Ribavirin (Continued)
ribavirin (Moderiba)		Chronic hepatitis C ▪In combination with peginterferon alfa-2a for the treatment of adults with CHC virus infection who have compensated liver disease and have not been previously treated with interferon alfa ▪Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm3 Moderiba should not be used as monotherapy; Safety and efficacy data are not available for treatment longer than 48 weeks; The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon
		Oral NSSA Inhibitor
daclatasvir (Daklinza)		Chronic hepatitis C genotype 1 or 3 in adults ▪In combination with sofosbuvir with or without ribavirin Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving daclatasvir in combination with sofosbuvir for 12 weeks
		Oral NS5B Polymerase Inhibitors
sofosbuvir (Sovaldi)		Chronic hepatitis C genotype 1, 2, 3, or 4 in adults ▪As a component of a combination antiviral treatment regimen Chronic hepatitis C genotypes 2 or 3 in pediatric patients (≥ 12 years of age or weighing ≥ 35 kg) ▪In combination with ribavirin

Hepatitis C – Indications

Drugs	Generic	Indications
Oral Combination Products		
glecaprevir/ pibrentasvir (Mavyret)		Chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults ▪Mavyret includes a combination of glecaprevir (an NS3/4A protease inhibitor) and pibrentasvir (an NS5A inhibitor) ▪Indicated for use without ribavirin ▪Indicated for use in treatment-experienced genotype 1 patients with prior regimen containing either an HCV NS5A inhibitor or an HCV NS3/4A PI, but not both
elbasvir/ grazoprevir (Zepatier)		Chronic hepatitis C genotype 1 or 4 in adults ▪Co-formulated fixed-dose tablet of elbasvir (an NS5A inhibitor) and grazoprevir (an NS3/4A protease inhibitor) ▪Indicated for use with or without ribavirin ▪Testing for NS5A resistance-associated polymorphisms needed for genotype 1a
ledipasvir/sofosbuvir (Harvoni)		Chronic hepatitis C genotype 1, 4, 5, or 6 in adults ▪Co-formulated fixed-dose tablet of ledipasvir (an NS5A inhibitor) and sofosbuvir (an NS5B Inhibitor) ▪Indicated for use with or without ribavirin Chronic hepatitis C genotypes 1, 4, 5, or 6 in pediatric patients (≥ 12 years of age or weighing ≥ 35 kg) ▪Indicated for use without ribavirin
ombitasvir/paritaprevir/ ritonavir + dasabuvir (Viekira Pak, Viekira XR)		Chronic hepatitis C genotype 1 in adults ▪Viekira Pak and Viekira XR include the combination of ombitasvir (an NS5A inhibitor), paritaprevir (a protease inhibitor), ritonavir (a potent CYP3A inhibitor to pharmacologically boost paritaprevir), and dasabuvir (an NS5B polymerase inhibitor) ▪Indicated for use with or without ribavirin, including in those with compensated cirrhosis
ombitasvir/paritaprevir/ ritonavir (Technivie)		Chronic hepatitis C genotype 4 in adults ▪Technivie includes the combination of ombitasvir (an NS5A inhibitor), paritaprevir (a protease inhibitor), and ritonavir (a potent CYP3A inhibitor to pharmacologically boost paritaprevir) ▪Indicated for use in combination with ribavirin

Hepatitis C – Indications

Drugs	Generic	Indications
Oral Combination Products (Continued)		
sofosbuvir/velpatasvir (Epclusa)		Chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults ▪ Epclusa includes a combination of sofosbuvir (an NS5B polymerase inhibitor) and velpatasvir (an NS5A inhibitor) ▪ Indicated for use with or without ribavirin
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi)		Chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults ▪ Vosevi includes a combination of sofosbuvir (an NS5B polymerase inhibitor), velpatasvir (an NS5A inhibitor), and voxilaprevir (an HCV NS3/4A protease inhibitor) ▪ Indicated for use in treatment-experienced genotype 1, 2, 3, 4, 5, and 6 patients with prior regimen containing an HCV NS5A inhibitor or genotype 1a or 3 patients with prior regimen containing sofosbuvir without an NS5A inhibitor ▪ Indicated for use without ribavirin

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
Dual Combination Therapy			
peginterferon alfa-2a (Pegasys) + ribavirin	Genotypes 1, 4: 180 mcg SC once weekly plus oral ribavirin (1,000 mg per day if < 75 kg or 1,200 mg per day if ≥ 75 kg)	48 weeks	SDV: 180 mcg/1 mL Autoinjector (ProClick): 135 mcg/0.5 mL, 180 mcg/0.5 mL Prefilled syringe: 180 mcg/0.5 mL
	Genotypes 2, 3: 180 mcg SC once weekly plus ribavirin 400 mg orally twice daily	24 weeks	
	Co-infection with HIV (regardless of genotype): 180 mcg SC once weekly plus ribavirin 400 mg orally twice daily	48 weeks	
	Age 5 to 17 years: 180 mcg/1.73 m^2 SC once weekly plus ribavirin 15 mg/kg/day orally with food in 2 divided doses	Genotype 1: 48 weeks	
		Genotypes 2 and 3: 24 weeks	
Dual Combination Therapy *(continued)*			
peginterferon alfa-2b (PEGIntron) + ribavirin	Age ≥ 18 years: 1.5 mcg/kg SC once weekly plus oral ribavirin 800 to 1,400 mg per day, based on body weight, in 2 divided doses	Genotype 1: 48 weeks	Kit: SDV with powder for injection (with diluent and syringes) 50 mcg
		Genotypes 2 and 3: 24 weeks	
	Age 3–17 years: 60 mcg/m2/week SC plus ribavirin 15 mg/kg/day orally with food in 2 divided doses Patients who reach their 18 years while receiving therapy should remain on the pediatric dosing regimen	Retreatment of prior treatment failure: 48 weeks, for all genotypes	

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
	Triple Combination Therapy		
daclatasvir (Daklinza)/ sofosbuvir ribavirin	60 mg orally once daily in combination with sofosbuvir 400 mg orally once daily with or without oral ribavirin Ribavirin should be added to the regimen for genotype 1 patients with decompensated cirrhosis (Child-Pugh B or C) and post-transplant patients Ribavirin should be added to the regimen for genotype 3 patients with compensated (Child-Pugh A) or decompensated (Child-Pugh B or C) cirrhosis and post-transplant patients Ribavirin dosing: Genotype 1 or 3 with Child-Pugh A: 1,000 mg/day orally for patients < 75 kg and 1,200 mg/day orally for patients ≥ 75 kg Genotype 1 or 3 with Child-Pugh B or C or post-transplantation: 600 mg/day orally and increasing to 1,000 mg/day as tolerated	Genotype 1 or 3: 12 weeks Dosing is the same regardless of HIV coinfection	daclatasvir 30 mg, 60 mg, and 90 mg†
sofosbuvir (Sovaldi) + peginterferon/ ribavirin	400 mg orally once daily plus weight-based oral ribavirin (1,000 mg per day if < 75 kg or 1,200 mg per day if ≥ 75 kg) and SC weekly peginterferon	Genotype 1 or 4: 12 weeks	sofosbuvir 400 mg tablet

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
Oral Combination Therapy			
elbasvir/ grazoprevir (Zepatier) ± ribavirin	Fixed-dose combination: elbasvir 50 mg/grazoprevir 100 mg orally once daily with or without food and with or without oral ribavirin Ribavirin should be added to the regimen for genotype 1a treatment-naïve or PegIFN/RBV-experienced patients with baseline NS5A polymorphisms, genotype 1a or 1b who are PegIFN/RBV/NS3/4A PI-experienced, and genotype 4 patients who are PegIFN/RBV-experienced Ribavirin dosing: weight based (range, 800 to 1,200 mg/day) administered orally in 2 divided doses with food; dosing adjusted for renal impairment	Genotype 1a (without baseline NS5A polymorphisms) or 1b– treatment naïve, PegIFN/RBV-experienced, PegIFN/RBV/NS3/4A PI-experienced: 12 weeks Genotype 1a (with baseline NS5A polymorphisms)‡– treatment naïve or PegIFN/RBV-experienced: 16 weeks Genotype 4– treatment naïve: 12 weeks Genotype 4– PegIFN/RBV-experienced: 16 weeks	elbasvir/ grazoprevir 50/100 mg fixed-dose tablet
glecaprevir/ pibrentasvir (Mavyret)	Fixed-dose combination: 3 glecaprevir 100 mg/pibrentasvir 40 mg tablets orally once daily with food	Genotypes 1, 2, 3, 4, 5, and 6 (treatment naïve without cirrhosis): 8 weeks Genotypes 1, 2, 3, 4, 5, and 6 (treatment naïve with compensated cirrhosis): 12 weeks Genotype 1 (treatment-experienced patient without cirrhosis or with compensated cirrhosis previously treated with a regimen containing an NS5A without prior treatment with an NS3/4A PI): 16 weeks Genotype 1 (treatment-experienced patient without cirrhosis or with compensated cirrhosis previously treated with a regimen containing an NS3/4A PI without prior treatment with an NS5A inhibitor): 12 weeks Genotype 1, 2, 4, 5 or 6 (treatment-experienced patient without cirrhosis previously treated with a regimen containing pegylated interferon, ribavirin, and/or sofosbuvir): 8 weeks Genotype 1, 2, 4, 5 or 6 (treatment-experienced patient with compensated cirrhosis previously treated with a regimen containing pegylated interferon, ribavirin, and/or sofosbuvir): 12 weeks Genotype 3 (treatment-experienced patient without cirrhosis or with compensated cirrhosis previously treated with a regimen containing pegylated interferon, ribavirin, and/or sofosbuvir): 16 weeks	100/40 mg fixed-dose tablet Dosing is the same regardless of HIV coinfection

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
Oral Combination Therapy (Continued)			
ledipasvir/ sofosbuvir (Harvoni) ± ribavirin	Fixed-dose combination: ledipasvir 90 mg/ sofosbuvir 400 mg orally once daily with or without oral ribavirin Ribavirin should be added to the regimen for genotype 1 treatment-naïve and treatment-experienced patients with decompensated cirrhosis (Child-Pugh B or C) Ribavirin should be added to the regimen for genotype 1 or 4 patients treatment-naïve and treatment-experienced liver transplant recipients with compensated (Child-Pugh A) cirrhosis or without cirrhosis Ribavirin dosing: ▪Noncirrhotic or Child-Pugh A cirrhosis post-transplantation: 1,000 mg/day orally for patients < 75 kg and 1,200 mg orally for patients ≥ 75 kg ▪Child-Pugh B or C: 600 mg orally once daily and increasing to 1,000 mg/day or 1,200 mg/day weight-based dosing as tolerated	Genotype 1 – treatment naïve (with compensated cirrhosis [Child-Pugh A] or without cirrhosis): 12 weeks Genotype 1 – treatment-experienced (without cirrhosis): 12 weeks Genotype 1 – treatment-experienced with compensated cirrhosis: 24 weeks** Genotype 1 – treatment-naïve or experienced (with decompensated cirrhosis): 12 weeks with ribavirin Genotype 1 or 4 – treatment naïve or experienced liver transplant recipients (with compensated cirrhosis or without cirrhosis): 12 weeks with ribavirin Genotypes 4, 5, or 6 – treatment-naïve or treatment-experienced with compensated cirrhosis or without cirrhosis: 12 weeks Patients co-infected with HIV/HCV should be treated in the same manner described above Genotype 1 – treatment-naïve pediatric patients without cirrhosis or with compensated cirrhosis: 12 weeks Genotype 1 – treatment-experienced†† pediatric patients without cirrhosis: 12 weeks Genotype 1 – treatment-experienced†† pediatric patients with compensated cirrhosis: 24 weeks Genotype 4, 5, or 6 – treatment-naïve or treatment-experienced†† pediatric patients without cirrhosis or with compensated cirrhosis: 12 weeks	90/400 mg fixed-dose tablet
ombitasvir/ paritaprevir/ ritonavir plus dasabuvir (Viekira Pak) ± ribavirin	Combination: 2 ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets orally once daily (in the morning) and 1 dasabuvir 250 mg tablet orally twice daily (morning and evening) with a meal ± weight-based oral ribavirin (< 75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg)	Genotype 1a (without cirrhosis): 12 weeks in combination with ribavirin Genotype 1a (with compensated cirrhosis): 24 weeks in combination with ribavirin Genotype 1b (without cirrhosis or with compensated cirrhosis): 12 weeks	ombitasvir/ paritaprevir/ ritonavir 12.5/75/50 mg fixed-dose tablet; dasabuvir 250 mg tablet

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
Oral Combination Therapy (Continued)			
ombitasvir/ paritaprevir/ ritonavir/ dasabuvir (Viekira XR) ± ribavirin	Combination: 3 ombitasvir/paritaprevir/ritonavir/ dasabuvir 8.33/50/33.3/200 mg tablets orally once daily with a meal ± weight-based oral ribavirin (< 75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg)	Genotype 1a (without cirrhosis): 12 weeks in combination with ribavirin Genotype 1a (with compensated cirrhosis): 24 weeks in combination with ribavirin Genotype 1b (without cirrhosis or with compensated cirrhosis): 12 weeks	ombitasvir/ paritaprevir/ ritonavir/ dasabuvir 8.33/50/33.3/200 mg fixed-dose tablet
ombitasvir/ paritaprevir/ ritonavir (Technivie) + ribavirin	Combination: 2 ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets orally once daily (in the morning) with a meal + weight-based oral ribavirin (< 75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg)	Genotype 4 (without cirrhosis or with compensated cirrhosis): 12 weeks	ombitasvir/ paritaprevir/ ritonavir 12.5/75/50 mg fixed-dose tablet
sofosbuvir (Sovaldi) + ribavirin	sofosbuvir 400 mg orally once daily plus weight-based oral ribavirin (adults: < 75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg; pediatric patients: < 47 kg = 15 mg/kg/day, 47 to 49 kg = 600 mg, 50 to 65 kg = 800 mg, 66 to 80 kg = 1,000 mg, ≥ 80 kg = 1,200 mg) Dosage reductions are not recommended	Genotype 2: 12 weeks Genotype 3: 24 weeks Patients with hepatocellular awaiting liver transplantation: up to 48 weeks or until time of liver transplant Genotype 1 patients who are interferon ineligible: 24 weeks HCV/HIV-1 co-infected patients with genotype 2: 12 weeks HCV/HIV-1 co-infected patients with genotype 3: 24 weeks Genotype 2 (pediatric patients ≥ 12 years of age or ≥ 35 kg): 12 weeks Genotype 3 (pediatric patients ≥ 12 years of age or ≥ 35 kg): 24 weeks	sofosbuvir 400 mg tablet

Hepatitis C – Dosing and Availability

Drugs	Dosage	Duration of Therapy	Availability
Oral Combination Therapy (Continued)			
sofosbuvir/velpatasvir (Epclusa) ± ribavirin	Fixed-dose combination: sofosbuvir 400 mg/velpatasvir 100 mg orally once daily with or without food and with or without oral ribavirin Ribavirin should be added to the regimen for patients with decompensated cirrhosis Ribavirin dosing is weight based: 1,000 mg for patients < 75 kg and 1,200 mg/day for patients ≥ 75 kg divided and administered orally twice daily with food	Genotypes 1, 2, 3, 4, 5, and 6 (without cirrhosis or with compensated cirrhosis): 12 weeks Genotypes 1, 2, 3, 4, 5, and 6 (with decompensated cirrhosis): 12 weeks in combination with ribavirin Dosing is the same regardless of HIV coinfection	sofosbuvir/ velpatasvir 400/100 mg fixed-dose tablet
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi)	Fixed-dose combination: sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg orally once daily with a meal	Genotypes 1, 2, 3, 4, 5, and 6 (treatment-experienced patients previously been treated with an HCV regimen containing an NS5A inhibitor): 12 weeks Genotypes 1a or 3 (treatment-experienced patients previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor): 12 weeks	400/100/100 mg fixed-dose tablet

Hepatitis C – Dosing and Availability

Drugs	Dosage	Availability
Ribavirin		
ribavirin (generics of Copegus)	As listed below for combination therapy slides	Tablet: 200 mg
ribavirin (Rebetol)		Capsule: 200 mg (generic only) Oral solution: 40 mg/mL
ribavirin (RibaPak)		Dose Packs (28-day supply): ▪ 600 mg/day (200 mg + 400 mg tablets in quantities of 7 or 28 tablets of each strength) ▪ 800 mg/day (400 mg tablets in quantities of 14 or 56) ▪ 1,000 mg/day (400 mg + 600 mg tablets in quantities of 7 or 28 tablets of each strength) ▪ 1,200 mg/day: (600 mg tablets in quantities of 14 or 56)
ribavirin (Ribasphere)		Capsule: 200 mg Tablets: 200 mg, 400 mg, 600 mg
ribavirin (Moderiba)		Tablets: 200 mg Dose Packs (7-day supply): ▪ 600 mg/day (200 mg + 400 mg tablets in quantities of 7 tablets of each strength) ▪ 800 mg/day (400 mg in quantities of 14) ▪ 1,000 mg/day (400 mg + 600 mg tablets in quantities of 7 tablets of each strength) ▪ 1,200 mg/day (600 mg tablets in quantities of 14)

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪ elbasvir/grazoprevir (without baseline NS5A RAVs)	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir*	8	Class I, Level B
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients **with compensated** cirrhosis:		
	▪ elbasvir/grazoprevir (without baseline NS5A RAVs)	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients without cirrhosis:		
	▪ elbasvir/grazoprevir (without baseline NS5A RAVs)	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients with compensated cirrhosis:		
	▪ elbasvir/grazoprevir (without baseline NS5A RAVs)	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	12	Class I, Level B

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Alternative Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir + weight-based RBV	12	Class I, Level A
	▪ daclatasvir + sofosbuvir	12	Class I, Level B
	▪ elbasvir/grazoprevir + weight-based RBV (baseline NS5A RAVs)	16	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	▪ elbasvir/grazoprevir + weight-based RBV (baseline NS5A RAVs)	16	Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis:		
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir + weight-based RBV	12	Class I, Level A
	▪ daclatasvir + sofosbuvir	12	Class I, Level B
	▪ elbasvir/grazoprevir + weight-based RBV (with baseline NS5A RAVs)	16	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	▪ ledipasvir/sofosbuvir + weight-based RBV	12	Class I, Level A
	▪ elbasvir/grazoprevir + weight-based RBV (with baseline NS5A RAVs)	16	Class I, Level B
Genotype 1b – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir*	8	Class I, Level B
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients **with compensated** cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1b – Recommended Treatments (Continued)			
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients **with compensated** cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	12	Class I, Level B
Genotype 1b – Alternative Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A
	▪ daclatasvir + sofosbuvir	12	Class I, Level B
	Patients **with compensated** cirrhosis:		
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis:		
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A
	▪ daclatasvir + sofosbuvir	12	Class I, Level B
	Patients **with compensated** cirrhosis:		
	▪ ledipasvir/sofosbuvir + weight-based RBV	12	Class I, Level A
	▪ paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype, unless noted) – Recommended Treatments			
Treatment-Experienced (previous failure of PEG-IFN / RBV + a HCV protease inhibitor [NS3], including telaprevir, boceprevir, or simeprevir)	Patients **without** cirrhosis: ▪ ledipasvir/sofosbuvir ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir Patients **with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir	 12 12 12 12 12	 Class I, Level A Class I, Level A Class IIa, Level B Class I, Level A Class IIa, Level B
Treatment-Experienced (previous failure of non-NS5A inhibitor, sofosbuvir-containing regimen)	Patients **without cirrhosis or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir (genotype 1a only) ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir (genotype 1b only)	 12 12 12	 Class I, Level A Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of any nonstructural protein 5A [NS5A] inhibitor)	Patients **without cirrhosis or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir	 12	 Class I, Level A
Genotype 1 (regardless of subtype, unless noted) – Alternative Treatments			
Treatment-Experienced (previous failure of PEG-IFN / RBV + a HCV protease inhibitor [NS3], including telaprevir, boceprevir, or simeprevir)	Patients **without** cirrhosis: ▪ elbasvir/grazoprevir + weight-based RBV (genotype 1b or 1a without baseline NS5A RAVs) ▪ elbasvir/grazoprevir + weight-based RBV (genotype 1a with baseline NS5A RAVs) Patients **with compensated** cirrhosis: ▪ ledipasvir/sofosbuvir + weight-based RBV ▪ elbasvir/grazoprevir + weight-based RBV (genotype 1b or 1a without baseline NS5A RAVs) ▪ elbasvir/grazoprevir + weight-based RBV (genotype 1a with baseline NS5A RAVs)	 12 16 12 12 16	 Class IIa, Level B Class IIa, Level B Class I, Level A Class IIa, Level B Class IIa, Level B

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype, unless noted) – Alternative Treatments (Continued)			
Treatment-Experienced (previous failure of non-NS5A inhibitor, sofosbuvir-containing regimen)	Patients **without** cirrhosis: ▪ ledipasvir/sofosbuvir + weight-based RBV (excluding simeprevir failures)	12	Class IIa, Level B
Treatment-Experienced (previous failure of any nonstructural protein 5A [NS5A] inhibitor)	Patients **without or with compensated** cirrhosis: ▪ glecaprevir/pibrentasvir (excluding prior therapy with NS3/4 protease inhibitor inclusive combination regimens)	16	Class IIa, Level B
Genotype 2 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients **with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir	8 12 12 12	Class I, Level A Class I, Level A Class I, Level A Class I, Level B
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients **with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir	8 12 12 12	Class I, Level A Class I, Level A Class I, Level A Class I, Level B
Treatment-Experienced (previous failure of sofosbuvir + RBV)	Patients **without cirrhosis or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir	12 12	Class I, Level B Class IIb, Level B

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 2 – Alternative Treatments			
Treatment-Naïve	Patients **without** cirrhosis: ▪ daclatasvir + sofosbuvir Patients **with compensated** cirrhosis: ▪ daclatasvir + sofosbuvir	12 16 to 24	Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ daclatasvir + sofosbuvir Patients **with compensated** cirrhosis: ▪ daclatasvir + sofosbuvir	12 16 to 24	Class IIa, Level B Class IIa, Level B
Genotype 3 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients **with compensated** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir	8 12 12 12	Class I, Level A Class I, Level A Class I, Level A Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ sofosbuvir/velpatasvir Patients **with compensated** cirrhosis: ▪ elbasvir/grazoprevir + sofosbuvir ▪ sofosbuvir/velpatasvir/voxilaprevir	12 12 12	Class I, Level A Class I, Level B Class IIb, Level B
Treatment-Experienced (previous failure of DAAs, including NS5A inhibitors)	Patients **without cirrhosis or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir ▪ sofosbuvir/velpatasvir/voxilaprevir + weight-based RBV (those with NS5A inhibitor failure and compensated cirrhosis)	12 12	Class I, Level A Class IIa, Level C

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 3 – Alternative Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪daclatasvir + sofosbuvir	12	Class I, Level A
	Patients **with compensated** cirrhosis:		
	▪sofosbuvir/velpatasvir/voxilaprevir (when Y93H present)	12	Class IIa, Level B
	▪daclatasvir + sofosbuvir ± weight-based RBV (RBV when Y93H present)	24	Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis:		
	▪daclatasvir + sofosbuvir (add RBV or use alternative regimen when Y93H present)	12	Class I, Level A
	▪glecaprevir/pibrentasvir	16	Class IIa, Level B
	▪sofosbuvir/velpatasvir/voxilaprevir (when Y93H present)	12	Class IIb, Level B
	Patients **with compensated** cirrhosis:		
	▪sofosbuvir/velpatasvir + weight-based RBV	12	Class I, Level B
	▪glecaprevir/pibrentasvir	16	Class IIa, Level B
Genotype 4 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	▪glecaprevir/pibrentasvir	8	Class I, Level A
	▪sofosbuvir/velpatasvir	12	Class I, Level A
	▪elbasvir/grazoprevir	12	Class IIa, Level B
	▪ledipasvir/sofosbuvir	12	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	▪sofosbuvir/velpatasvir	12	Class I, Level A
	▪glecaprevir/pibrentasvir	12	Class I, Level B
	▪elbasvir/grazoprevir	12	Class IIa, Level B
	▪ledipasvir/sofosbuvir	12	Class IIa, Level B

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 4 – Recommended Treatments			
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir ▪ elbasvir/grazoprevir (without on-treatment failure only) ▪ ledipasvir/sofosbuvir Patients **with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir ▪ elbasvir/grazoprevir (without on-treatment failure only) ▪ glecaprevir/pibrentasvir	 12 8 12 12 12 12 12	 Class I, Level A Class I, Level B Class IIa, Level B Class IIa, Level B Class I, Level A Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of DAAs, including NS5A inhibitors)	Patients **without or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir	 12	 Class I, Level A
Genotype 4 – Alternative Treatments			
Treatment-Naïve	Patients **without or with compensated** cirrhosis: ▪ paritaprevir/ritonavir/ombitasvir + weight-based RBV	 12	 Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ paritaprevir/ritonavir/ombitasvir + weight-based RBV ▪ elbasvir/grazoprevir + weight-based RBV (those with on-treatment failure) Patients **with compensated** cirrhosis ▪ paritaprevir/ritonavir/ombitasvir + weight-based RBV ▪ elbasvir/grazoprevir + weight-based RBV (those with on-treatment failure) ▪ ledipasvir/sofosbuvir + weight-based RBV	 12 16 12 16 12	 Class I, Level A Class IIa, Level B Class I, Level A Class IIa, Level B Class IIa, Level B

Hepatitis C – Guidelines (AASLD/IDSA HCV Guidelines, 2017)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 5/6 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir ▪ ledipasvir/sofosbuvir Patients **with compensated** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir ▪ ledipasvir/sofosbuvir	 8 12 12 12 12 12	 Class I, Level A Class I, Level B Class IIa, Level B Class I, Level A Class I, Level B Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir ▪ ledipasvir/sofosbuvir Patients **with compensated** cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir ▪ ledipasvir/sofosbuvir	 8 12 12 12 12 12	 Class IIa, Level B Class IIa, Level B Class IIa, Level B Class I, Level B Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of DAAs, including NS5A inhibitors)	Patients **without or with compensated** cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir	 12	 Class IIa, Level B

Magellan Rx MANAGEMENT℠

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Multiple Sclerosis

Overview of Disease State – Multiple Sclerosis

- Multiple sclerosis (MS) is a complex human autoimmune-type inflammatory disease of the central nervous system (CNS)
  - More than 2.3 million people worldwide have MS
  - Multiple sclerosis occurs most commonly in whites, with rare cases in African-Americans and Asian-Americans

- Although the etiology is predominantly unknown, MS is characterized pathologically by demyelination and subsequent axonal degeneration
  - The nerve degeneration associated with MS can result in a wide variety of symptoms, including sensory disturbances (numbness, paresthesias, burning, and pain) in the limbs, optic nerve dysfunction, ataxia, fatigue, and bladder, bowel, and sexual dysfunction
  - Severe cases may result in partial or complete paralysis
  - While cognitive impairment occurs in approximately 50% of people with MS, only 10% experience serious intellectual deterioration

- MS can be categorized as either relapsing-remitting MS (observed in 85% to 90% of patients) or primary progressive MS (observed in 10% of patients)
  - Relapses or “attacks” typically present subacutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually dissipating

Overview of Disease State – Multiple Sclerosis

- The clinical course of MS falls into 1 of the following categories, with the potential to progress from less severe to more serious types:
  - **Relapsing-remitting MS (RRMS):** Clearly defined, self-limited attacks of neurologic dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often, but not always, complete
  - **Primary progressive MS (PPMS):** Nearly continuous worsening of disease not interrupted by distinct relapses; some of these individuals have occasional plateaus and temporary minor improvements
  - **Secondary progressive MS (SPMS):** Relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus; most patients eventually convert to progressive MS
  - **Progressive-relapsing MS (PRMS):** Progressive disease from onset, with clear, acute relapses that may or may not resolve with full recovery; unlike RRMS, the periods between relapses are characterized by continuing disease progression
  - **Clinically isolated syndromes (CIS):** the first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours. Patients with MRI-detected brain lesions consistent with MS are at high risk of developing MS

Multiple Sclerosis – Indications

Drugs	Generic	Indications
alemtuzumab (Lemtrada)		Relapsing forms of multiple sclerosis; due to its safety profile, the use of alemtuzumab should generally be reserved for patients who have had an inadequate response to 2 or more drugs indicated for the treatment of multiple sclerosis
dalfampridine (Ampyra)	x	Improve walking in patients with multiple sclerosis, demonstrated by an increase in walking speed
dimethyl fumarate (Tecfidera)		Relapsing forms of multiple sclerosis
fingolimod (Gilenya)		Relapsing forms of multiple sclerosis in patients 10 years of age and older
glatiramer acetate (Copaxone)	x	Relapsing forms of multiple sclerosis
interferon ß-1a IM (Avonex)		Relapsing forms of multiple sclerosis – to delay accumulation of disability and to decrease frequency of clinical exacerbations
interferon ß-1a SC (Rebif)		
interferon ß-1a SC (pegylated) (Plegridy)		Relapsing forms of multiple sclerosis
interferon ß-1b (Betaseron)		Relapsing forms of multiple sclerosis – to reduce frequency of exacerbations
interferon ß-1b (Extavia)		Relapsing forms of multiple sclerosis – to reduce frequency of exacerbations
natalizumab (Tysabri)		Relapsing forms of multiple sclerosis Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies, including other biologic agents
ocrelizumab (Ocrevus)		Relapsing multiple sclerosis (RMS) or primary progressive multiple sclerosis (PPMS)
teriflunomide (Aubagio)		Relapsing forms of multiple sclerosis

Multiple Sclerosis – Dosing and Availability

Drugs	Dosage	Comments	Availability
alemtuzumab (Lemtrada)	12 mg per day by intravenous (IV) infusion over 4 hours for 2 courses of therapy; course 1 is for 5 days and course 2 is for 3 days 1 year after the first course	• Refrigerate • May be stored at room temperature (25oC) for up to 8 hours before administration Protect from light	Single use vial: 12 mg/1.2 mL solution
dalfampridine (Ampyra)	10 mg by mouth twice daily about 12 hours apart	--	Extended-release (ER) tablets: 10 mg
dimethyl fumarate (Tecfidera)	120 mg by mouth twice daily for 7 days and then 240 mg twice daily	• Should not be crushed, chewed, or sprinkled on food • Can be taken with or without food; administration with food may reduce the incidence of flushing	Delayed release capsules: 120 mg and 240 mg; 30 day starter pack
fingolimod (Gilenya)	Adults and pediatric patients ≥ 10 years weighing > 40 kg: 0.5 mg by mouth once daily; Pediatric patients ≥ 10 years and weighing ≤ 40 kg: 0.25 mg by mouth once daily	--	Capsules: 0.25 mg, 0.5 mg capsules
glatiramer acetate (Copaxone)	20 mg SC once daily 40 mg SC 3 times weekly (at least 48 hours apart)	• Refrigerate • May be stored at room temperature for up to 1 month (refrigeration preferred)	Single-dose prefilled syringes: 20 mg/mL, 40 mg/mL (brand and generic) 20 mg and 40 mg strengths are not interchangeable

Multiple Sclerosis – Dosing and Availability

Drugs	Dosage	Comments	Availability
IFNß-1a (Avonex)	30 mcg IM once weekly	• Refrigerate; may be stored at room temperature (25oC) for up to 7 days • Use immediately following reconstitution; however, may be refrigerated for up to 6 hours • Protect from light	Powder for injection vial with diluent: 30 mcg
IFNß-1a (Avonex prefilled syringe)		• Refrigerate; allow to come to room temperature before use (~30 minutes) • May be stored at room temperature (≤ 25oC) for up to 7 days Protect from light	Prefilled syringes: 30 mcg/0.5 mL
IFNß-1a (Avonex pen)			Prefilled autoinjectors/pens: 30 mcg/0.5 mL
IFNß-1a (Rebif)	4.4 mcg or 8.8 mcg SC 3 times weekly, titrated over 4 weeks up to 22 mcg or 44 mcg SC 3 times weekly	• Refrigerated • May be stored at or below room temperature for up to 30 days away from heat and light	Prefilled syringes: 22 mcg/0.5 mL, 44 mcg/0.5 mL, titration pack
IFNß-1a (Rebif Rebidose)			Prefilled autoinjector: 22 mcg/0.5 mL, 44 mcg/0.5 mL, titration pack
IFN ß-1a SC (pegylated) (Plegridy)	125 mcg SC every 14 days, titrated over 4 weeks with a dose of 63 mcg at initiation and 94 mcg 2 weeks later	• Refrigerate • May be stored at room temperature for up to 30 days • Allow to come to room temperature before use (~30 minutes) • Protect from light	Prefilled syringes or autoinjector pens: 125 mcg, starter pack (63 mcg and 94 mcg)

Multiple Sclerosis – Dosing and Availability

Drugs	Dosage	Comments	Availability
IFNß-1b (Betaseron)	0.0625 mg SC every other day; Increased over a 6-week period to 0.25 mg SC every other day	• Store at room temperature prior to reconstitution • Stable refrigerated for 3 hours after reconstitution	Powder for injection, vial with diluent: 0.3 mg May be used with or without the Betaconnect autoinjector
IFNß-1b (Extavia)	0.0625 mg SC every other day Increased over a 6-week period to 0.25 mg SC every other day	• Store at room temperature prior to reconstitution • Stable refrigerated for 3 hours after reconstitution	Powder for injection vial with diluent: 0.3 mg
natalizumab (Tysabri)	300 mg IV infusion over 1 hour every 4 weeks	• Observe for 1 hour following infusion completion • Discontinue infusion if hypersensitivity occurs • Prescribers must be enrolled in MS TOUCH® program • Preparation procedures for dilution are described in the prescribing information	Single-use vial: 300 mg/15 mL
ocrelizumab (Ocrevus)	Initial dose: 300 mg as an IV infusion over at least 2.5 hours, followed 2 weeks later by a second 300 mg IV infusion Maintenance dose: 600 mg as an IV infusion over at least 3.5 hours every 6 months beginning 6 months after the first infusion	• Observe for 1 hour following information • Discontinue infusion if life-threatening or disabling hypersensitivity occurs • Premedicate with a corticosteroid and antihistamine with or without an antipyretic prior to infusion as detailed in the prescribing information • Preparation procedures for dilution and recommended infusion rate guidelines (including rates based on adverse effects/tolerability during infusion) are described in the prescribing information	Single-dose vial: 300 mg/10 mL
teriflunomide (Aubagio)	7 mg or 14 mg by mouth once daily	--	Tablets: 7 mg, 14 mg tablets

Multiple Sclerosis – Guidelines

American Academy of Neurology (AAN), 2018

- The guidelines discuss patient counseling, including patient readiness, medication adherence, and treatment-related adverse effects; therapy initiation; and treatment selection, switching, and discontinuation
- Notably, they clarify that prescribers should counsel patients with MS that treatments are intended to reduce relapses and new MRI lesion activity; they are not intended for symptom improvement
- Treatment Options
  - Clinicians should offer disease-modifying therapy (DMT) to people with relapsing forms of MS with recent clinical relapses or MRI activity (Level B)
  - After discussing the risks and benefits, clinicians should prescribe DMT to people with a single clinical demyelinating event and 2 or more brain lesions characteristic of MS in those who decide they want this therapy (Level B)
  - Clinicians should prescribe alemtuzumab, fingolimod, or natalizumab for people with highly active MS (Level B)
  - Clinicians may recommend azathioprine or cladribine for people with relapsing forms of MS who do not have access to approved DMTs (Level C), but they should not prescribe mitoxantrone to people with MS unless the potential therapeutic benefits greatly outweigh the risks (Level B)
  - Similarly, natalizumab treatment should only be initiated in people with MS with positive anti-JCV antibody indexes above 0.9 when there is a reasonable chance of benefit compared with the risk of progressive multifocal leukoencephalopathy (PML) (Level C)
  - For PPMS, clinicians should offer ocrelizumab to those who are likely to benefit unless the risks outweigh the benefit (Level B)

Multiple Sclerosis – Guidelines

American Academy of Neurology (AAN), 2018

- Regarding treatment switching, clinicians should evaluate disease activity, adherence, adverse effects, and pharmacology when switching DMTs in people with breakthrough disease activity during DMT use

- A change to non-injectable or less frequently injected treatments or a change due to adverse effects impacting adherence may be considered based on patient feedback (both Level B)
  - A switch (or dosage adjustment) may be warranted due to laboratory abnormalities, pregnancy, PML risk, malignancy, serious infections, and in those with select antibodies (all Level B)
  - Clinicians should then advocate that stable MS patients (e.g., no relapses, no disability progression, stable imaging) continue their current treatment unless a trial off therapy is warranted by both the prescriber and patient (Level B); however, discontinuation may be advised in patients with SPMS who do not have ongoing relapses (or gadolinium-enhanced lesions on MRI activity) and have not been ambulatory (Expanded Disability Status Scale [EDSS] ≥ 7) for ≥ 2 years

Multiple Sclerosis – Guidelines

The International Pediatric MS Study Group and American Academy of Neurology (AAN), 2016

- Recommend that clinicians treat children with MS in order to prevent relapses, prevent new lesions, and delay disability, which is of particular concern in pediatrics since they have a higher relapse rate more significant inflammation on MRI
- DMT use in pediatric MS remains off-label in the majority of countries
- They state that IFNß and glatiramer should be considered standard of care in this population and that treatment should be started early
  - Although the clinician should counsel families regarding realistic expectations, a treatment switch may be warranted if there is inadequate or suboptimal response
  - Clinical trials may be available and useful for those who require escalating or emerging treatments

- Note: these were published prior to the FDA approval of fingolimod for relapsing forms of MS in pediatric patients ≥ 10 years of age